

PTO/SB/08a (05-03)

Approved for use through 04/30/2003. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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Substitute for form 1449A/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet 1 of 10

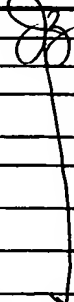
Complete If Known

Application Number	10/701,012
Filing Date	November 4, 2003
First Named Inventor	Muthiah Manoharan
Art Unit	Not Yet Assigned
Examiner Name	Not Yet Assigned 1635
Attorney Docket Number	ISIC0010-101 (CHEM0004US.P1)

U.S. PATENT DOCUMENTS

Examiner Initials *	Cite No. ¹	Document Number		Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number - Kind Code ² (if known)				
83	AA	US-5,898,031		04-27-1999	CROOKE	
	AB	US- 6,107,094		08-22-2000	CROOKE	
	AC	US- 5,543,507		08-06-1996	COOK ET AL.	
	AD	US- 6,005,093		12-21-1999	WOOD ET AL.	
	AE	US- 5,082,934		01-21-1992	SABA ET AL.	
	AF	US- 6,406,850		06-18-2002	VOLKERS ET AL.	
	AG	US- 6,303,799		10-16-2001	CHENG ET AL.	
	AH	US- 6,232,463		05-15-2001	COOK ET AL.	
	AI	US- 6,143,877		11-07-2000	MEYER ET AL.	
	AJ	US- 6,072,046		06-06-2000	REED ET AL.	
	AK	US- 5,824,796		10-20-1998	PETRIE ET AL.	
	AL	US- 5,811,534		09-22-1998	COOK ET AL.	
	AM	US- 5,767,259		06-16-1998	ALBAGLI ET AL.	
	AN	US- 5,719,271		02-17-1998	COOK ET AL.	
	AO	US- 5,714,360		02-03-1998	SWAN ET AL.	
	AP	US- 5,681,941		10-28-1997	COOK ET AL.	
	AQ	US- 5,659,022		08-19-1997	KUTYAVIN ET AL.	
	AR	US- 4,826,967		05-02-1989	GLASS	
	AS	US- 4,123,610		10-31-1978	SUMMERTON ET AL.	
	✓	AT	US- 2002/0012915		01-31-2002	VOLKERS ET AL.

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document		Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ - Number ⁴ - Kind Code ⁵ (if known)					
	AU	WO01/48183		07-05-2001	DEVGEN NV		
	AV	WO00/44895		08-03-2000	KREUTZER		
	AW	WO00/49035		08-24-2000	GEN HOSP.		
	AX	WO00/63364		10-26-2000	AMER. HOME PRODUCTS		
	AY	WO01/36641		05-25-2001	CHIRON CORP		
	AZ	WO01/36646		05-25-2001	CANCER RES. CAMPAIGN		
	BA	WO99/32619		07-01-1999	CARNEGIE INST OF WASH.		
	BB	WO00/44914		08-03-2000	MED. COLLEGE OF GEORGIA		
	BC	WO01/29058		04-26-2001	UNIV. OF MASS.		

Examiner Signature

83

Date Considered

4 / 28 / 06

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kind Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

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If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Substitute for form 1449A/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				Application Number	10/701,012
				Filing Date	November 4, 2003
				First Named Inventor	Muthiah Manoharan
				Art Unit	Not Yet Assigned
				Examiner Name	Not Yet Assigned
Sheet	2	of	10	Attorney Docket Number	ISIC0010-101 (CHEM0004US.P1)

U.S. PATENT DOCUMENTS					
Examiner Initials *	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
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23	BD	US- 5,688,941	11-18-1997	COOK ET AL.	
	BE	US- 5,714,166	06-06-1996	TOMALIA ET AL.	
	BF	US- 6,153,737	11-28-2000	MANOHARAN	
	BG	US- 6,172,208	01-09-1991	COOK	
	BH	US- 6,300,319	10-09-2001	MANOHARAN	
	BI	US- 6,335,434	01-01-2002	GUZAEV ET AL.	
	BJ	US- 6,335,437	01-01-2002	MANOHARAN	
	BK	US- 6,395,437	05-28-2002	WOLLESEN	
	BL	US- 6,444,486	09-03-2002	KWAK ET AL.	
	BM	US- 6,486,308	11-26-2002	KUTYAVIN	
	BN	US- 6,525,031	02-25-2003	MANOHARAN	
	BO	US- 6,528,631	03-04-2003	COOK ET AL.	
	BP	US- 6,559,279	05-06-2003	MANOHARAN ET AL.	
	BQ	US- 5,272,250	12-21-1993	SPIELVOGEL	
	BR	US- 5,292,873	03-08-1994	ROKITA ET AL.	
	BS	US- 5,317,098	03-31-1994	SHIZUYA ET AL.	
	BT	US- 5,371,241	12-06-1994	BRUSH	
	BU	US- 5,391,723	02-21-1995	PRIEST	

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23	BV	WO01/75164	10-11-2001	WHITEHEAD INST.		
	BW	WO91/10671	07-25-1991	ISIS PHARM.		
	BX	WO96/28438	09-19-1996	NAXCOR		
	BY	WO93/07883	04-29-1993	ISIS PHARM.		

Examiner Signature		Date Considered	4/28/06
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JP	BZ	US- 5,416,203	05-16-1995	LETSINGER ET AL.	
	CA	US- 5,451,463	09-19-1995	NELSON ET AL.	
	CB	US- 5,510,475	04-23-1996	AGRAWAL ET AL.	
	CC	US- 5,512,667	04-30-1996	REED ET AL.	
	CD	US- 5,514,785	05-07-1996	VAN NESS ET AL.	
	CE	US- 5,565,552	10-15-1996	MAGDA ET AL.	
	CF	US- 5,567,810	10-22-1996	WEIS ET AL.	
	CG	US- 5,574,142	11-12-1996	MEYER ET AL.	
	CH	US- 5,585,481	12-17-1996	ARNOLD ET AL.	
	CI	US- 5,587,371	12-24-1996	SESSLER ET AL.	
	CJ	US- 5,595,726	01-21-1997	MAGDA ET AL.	
	CK	US- 5,597,696	01-28-1997	LINN ET AL.	
	CL	US- 5,599,923	02-04-1997	SESSLER ET AL.	
	CM	US- 5,599,928	02-04-1997	HEMMI ET AL.	
	CN	US- 5,672,662	09-30-1997	HARRIS ET AL.	
	CO	US- 4,587,044	05-06-1986	MILLER ET AL.	
CP	US- 4,605,735	08-12-1986	MIYOSHI ET AL.		
	CQ	US- 4,667,025	05-19-1987	MIYOSHI ET AL.	

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83	CR	US- 4,762,779	08-09-1988	SNITMAN	
	CS	US- 4,789,737	12-06-1988	MIYOSHI ET AL.	
	CT	US- 4,824,941	04-25-1989	GORDON ET AL.	
	CU	US- 4,835,263	05-30-1989	NGUYEN ET AL.	
	CV	US- 4,876,335	10-24-1989	YAMANE ET AL.	
	CW	US- 4,904,582	02-27-1990	TULLIS	
	CX	US- 4,958,013	09-18-1990	LETSINGER	
	CY	US- 5,082,830	01-21-1992	BRAKEL ET AL.	
	CZ	US- 5,112,963	05-12-1992	PIELES ET AL.	
	DA	US- 5,214,136	05-25-1993	LIN ET AL.	
	DB	US- 5,149,782	09-22-1992	CHANG ET AL.	
	DC	US- 5,245,022	09-14-1993	WEIS ET AL.	
	DD	US- 5,254,469	10-19-1993	WARREN III ET AL.	
	DE	US- 5,258,506	11-02-1993	URDEA ET AL.	
	DF	US- 5,262,536	11-16-1993	HOBBS ET AL.	
	DG	US- 3,687,808	08/29/1972	MERIGAN et al.	
	DH	US- 6,395,492	05-28-2002	MANOHARAN ET AL.	
	DI	US- 4,828,979	05-09-1989	KLEVAN ET AL.	
	DJ	US- 4,948,882	08-14-1990	RUTH	
DK	US- 5,218,105	06-08-1993	COOK ET AL.		

[illegible]

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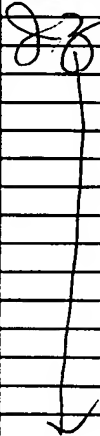
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	DL	US- 5,525,465	06-11-1996	HARALAMBIDIS	
	DM	US- 5,541,313	07-30-1996	RUTH	
	DN	US- 5,545,730	08-13-1996	URDEA ET AL.	
	DO	US- 5,552,538	09-03-1996	URDEA ET AL.	
	DP	US- 5,578,717	11-26-1996	URDEA ET AL.	
	DQ	US- 5,580,731	12-03-1996	CHANG ET AL.	
	DR	US- 5,591,584	01-07-1997	CHANG ET AL.	
	DS	US- 5,109,124	04-28-1992	RAMACHANDRAN	
	DT	US- 5,118,802	06-02-1992	SMITH ET AL.	
	DU	US- 5,138,045	08-11-1992	COOK ET AL.	
	DV	US- 5,414,077	05-09-1995	LIN ET AL.	
	DW	US- 5,486,603	01-23-1996	BUHR	
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	DY	US- 5,578,718	11-26-1996	COOK	
	DZ	US- 5,608,046	03-04-1997	COOK ET AL.	

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		Examiner Name	Not Yet Assigned
Sheet 6 of 10	Attorney Docket Number	ISIC0010-101 (CHEM0004US.P1)	

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS			
Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
J3	EA	SUMMERTON, J., "Sequence-Specific Crosslinking Agents for Nucleic Acids: Design and Functional Group Testing," <i>J. Theor. Biol.</i> (1979) 78:61-75.	
	EB	MEYER, Jr., R.B., et al., "Efficient, Specific Cross-Linking and Cleavage of DNA by Stable, Synthetic Complementary Oligodeoxynucleotides," <i>J. Am. Chem. Soc.</i> (1989) 111(22):8517-8519.	
	EC	WEBB, T. R., et al., "Hybridization triggered cross-linking of deoxyoligonucleotides," <i>Nucleic Acids Res.</i> (1986) 14(19):7661-7674.	
	ED	MATTEUCCI, M. D., et al., "Synthesis and Crosslinking Properties of a Deoxyoligonucleotide Containing N ⁶ ,N ⁶ -Ethanodeoxyadenosine," <i>Tetrahedron Lett.</i> (1987) 28(22):2469-2472.	
	EE	FERENTZ, A. E., et al., "Disulfide Cross-Linked Oligonucleotides," <i>J. Am. Chem. Soc.</i> (1991) 113(10):4000-4002.	
	EF	MANOHARAN, M., "Designer Antisense Oligonucleotides: Conjugation Chemistry and Functionality Placement," <i>Antisense Research and Applications</i> , Crooke and LeBleu, eds., CRC Press Boca Raton, FL, 1993, pp 303-349.	
	EG	CARMELL, M.A., et al., "The Argonaute family: tentacles that reach into RNAi, developmental control, stem cell maintenance, and tumorigenesis," <i>Gene Dev.</i> (2002) 16(21):2733-2742.	
	EH	LIN, K.-Y., et al., "A Cytosine Analogue Capable of Clamp-Like Binding to a Guanine in Helical Nucleic Acids," <i>J. Am. Chem. Soc.</i> (1998) 120(33):8531-8532.	
	EI	FLANAGAN, W. M., et al., "Cellular penetration and antisense activity by a phenoxazine-substituted heptanucleotide," <i>Nature Biotechnol.</i> (1999) 17(1):48-52.	
	EJ	MANOHARAN, M., "Oligonucleotide Conjugates in Antisense Technology," <i>Antisense Drug Technology, Principles, Strategies and Applications</i> , S.T. Crooke, ed., Dekker, Inc., 2001, pp 391-467.	
EK	MANOHARAN, M., "Oligonucleotide Conjugates as Potential Antisense Drugs with Improved Uptake, Biodistribution, Targeted Delivery, and Mechanism of Action," <i>Antisense Nucleic Acid Drug Dev.</i> (2002) 12(2):103-128.		

Examiner Signature	J3	Date Considered	4/28/06
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		Attorney Docket Number	ISIC0010-101 (CHEM0004US.P1)
Sheet	7	of	10

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Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
83	EL	MARTINEZ, J., et al., "Single-Stranded Antisense siRNAs Guide Target RNA Cleavage in RNAi," <i>Cell</i> (2002) 110:563-574.	
	EM	BOUTLA, A., et al., "Short 5'-phosphorylated double-stranded RNAs induce RNA interference in <i>Drosophila</i> ," <i>Curr. Biol.</i> (2001) 11:1776-1780.	
	EN	SCHWARZ, D. S., et al., "Evidence that siRNAs Function as Guides, Not Primers, in the <i>Drosophila</i> and Human RNAi Pathways," <i>Mol. Cell.</i> (2002) 10:537-548.	
	EO	CHIU, Y.-L., et al., "RNAi in Human Cells: Basic Structural and Functional Features of Small Interfering RNA," <i>Mol. Cell</i> (2002) 10:549-561.	
	EP	LIN, M., et al., "Inhibition of collagenase type I expression by psoralen antisense oligonucleotides in derman fibroblasts," <i>FASEB J.</i> (1995) 9(13):1371-1377.	
	EQ	MARUENDA, H., et al., "Antisense Sequence-Directed Cross-Linking of DNA Oligonucleotides by Mitomycin C," <i>Bioconj. Chem.</i> (1996) 7(5):541-544.	
	ER	MARUENDA, H., et al., "Antisense sequence-directed cross-linking of RNA oligonucleotides by mitomycin," <i>Anti-Cancer Drug Design</i> (1997) 12:473-479.	
	ES	HU, N., et al., "Design, Synthesis, and Evaluation of Mitomycin-Tethered Phosphorothioate Oligodeoxynucleotides," <i>Bioconj. Chem.</i> (1996) 7(6):659-669.	
	ET	COHEN, G.L., et al., "Sequence Dependent Binding of <i>cis</i> -Dichlorodiammineplatinum(II) to DNA," <i>J. Am. Chem. Soc.</i> (1980) 102(7):2487-2488.	
	EU	GRINEVA, N. I., et al., "Complementarily Addressed Modification of rRNA with p-(Chloroethylmethylamino)benzylidene Hexanucleotides," <i>FEBS Lett.</i> (1973) 32(2):351-355.	
	EV	SUMMERTON, J., et al., "Sequence-specific Crosslinking Agents for Nucleic Acids," <i>J. Mol. Biol.</i> (1978) 122(2):145-162.	

Examiner Signature		Date Considered	4/28/06
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Substitute for form 1449A/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	10/701,012
				Filing Date	June 26, 2003
				First Named Inventor	Muthiah Manoharan
				Group Art Unit	Not Yet Assigned
				Examiner Name	Not Yet Assigned
(use as many sheets as necessary)				Attorney Docket Number	ISIC0010-101 (CHEM0004US.P1)
Sheet	8	of	10		

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Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
J3	EW	TUSCHL, T., et al., "Targeted mRNA degradation by double-stranded RNA in vitro," <i>Genes Dev.</i> (1999) 13(24):3191-3197.	
	EX	ELBASHIR, S. M., et al., "RNA interference is mediated by 21- and 22-nucleotide RNAs," <i>Genes Dev.</i> (2001) 15(2):188-200.	
	EY	ELBASHIR, S. M., et al., "Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells," <i>Nature</i> (2001) 411(6836):494-498.	
	EZ	LIPARDI, C., et al., "RNAi as Random Degradative PCR: siRNA Primers Convert mRNA into dsRNAs that Are Degraded to Generate New siRNAs," <i>Cell</i> (2001) 107:297-307.	
	FA	NISHIKURA, K., "A Short Primer on RNAi: RNA-Directed RNA Polymerase Acts as a Key Catalyst," <i>Cell</i> (2001) 107:415-418.	
	FB	SIJEN, T., et al., "On the Role of RNA Amplification in dsRNA-Triggered Gene Silencing," <i>Cell</i> (2001) 107:465-476.	
	FC	TIJSTERMAN, M., et al., "RNA Helicase MUT-14-Dependent Gene Silencing Triggered in <i>C. elegans</i> by Short Antisense RNAs," <i>Science</i> (2002) 295(5555):694-697.	
	FD	ELBASHIR, S. M., et al., "Functional anatomy of siRNAs for mediating efficient RNAi in <i>Drosophila melanogaster</i> embryo lysate," <i>EMBO J.</i> (2001) 20(23):6877-6888.	
	FE	PARRISH, S., et al., "Functional Anatomy of a dsRNA Trigger: Differential Requirement for the Two Trigger Strands in RNA Interference," <i>Mol. Cell.</i> (2000) 6:1077-1087.	
	FF	MELLITZER, G., et al., "Spatial and temporal 'knock down' of gene expression by electroporation of double-stranded RNA and morpholinos into early postimplantation mouse embryos," <i>Mech. Devel.</i> (2002) 118(1-2):57-63.	
FG	BASS, B. L., et al., "Double-Stranded RNA as a Template for Gene Silencing," <i>Cell</i> (2000) 101:235-238.		

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				Application Number	10/701,012
				Filing Date	November 4, 2003
				First Named Inventor	Muthiah Manoharan
				Group Art Unit	Not Yet Assigned
				Examiner Name	Not Yet Assigned
Sheet	09	Of	10	Attorney Docket Number	ISIC0010-101 (CHEM0004US.P1)

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Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
93	FH	WAGNER, D., et al., "Preparation and Synthetic Utility of Some Organotin Derivatives of Nucleosides," <i>J. Org. Chem.</i> (1974) 39(1):24-30.	
	FI	NAPOLI, C., et al., "Introduction of a Chimeric Chalcone Synthase Gene into Petunia Results in Reversible Co-Suppression of Homologous Genes in trans," <i>Plant Cell</i> (1990) 2:279-289.	
	FJ	JORGENSEN, R. A., et al., "Chalcone synthase cosuppression phenotypes in petunia flowers: comparison of sense vs. antisense constructs and single-copy vs. complex T-DA sequences," <i>Plant. Mol. Biol.</i> (1996) 31:957-973.	
	FK	COGONI, C., et al., "Post-transcriptional gene silencing across kingdoms," <i>Curr. Opin. Genes Dev.</i> (2000) 10(6):638-643.	
	FL	GURA, T., "A silence that speaks volumes," <i>Nature</i> (2000) 404:804-808.	
	FM	GUO, S., et al., "par-1, a Gene Required for Establishing Polarity in C. elegans Embryos, Encodes a Putative Ser/Thr Kinase That is Asymmetrically Distributed," <i>Cell</i> (1995) 81:611-620.	
	FN	FIRE, A., et al., "Potent and specific genetic interference by double-stranded RNA in <i>Caenorhabditis elegans</i> ," <i>Nature</i> (1998) 391:806-811.	
	FO	TIMMONS, L., et al., "Specific interference by ingested dsRNA," <i>Nature</i> (1998) 395:854.	
	FP	TIMMONS, L., et al., "Ingestion of bacterially expressed dsRNAs can produce specific and potent genetic interference in <i>Caenorhabditis elegans</i> ," <i>Gene</i> (2001) 263:103-112.	
	✓	FQ	TABARA, H., et al., "RNAi in C. elegans: Soaking in the Genome Sequence," <i>Science</i> (1998) 282:430-431.

Examiner Signature		Date Considered	4/28/06
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Substitute for form 1449A/PTO		Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)		Application Number	10/701,012
		Filing Date	June 26, 2003
		First Named Inventor	Muthiah, Manoharan
		Group Art Unit	Not Yet Assigned
		Examiner Name	Not Yet Assigned
Sheet 10 of 10	Attorney Docket Number	ISIC0010-101 (CHEM0004US.P1)	

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J3	FR	MONTGOMERY, M. K., et al., "RNA as a target of double-stranded RNA-mediated genetic interference in <i>Caenorhabditis elegans</i> ," <i>Proc. Natl. Acad. Sci. USA</i> (1998) 95(26):15502-15507.	
	FS	BRANTL, S., "Antisense-RNA Regulation and RNA Interference," <i>Biochim. Biophys. Acta.</i> (2002) 1575:15-25.	
	FT	ENDO, M., et al., "Control of A Double Helix DNA Assembly by Use of Cross-Linked Oligonucleotides," <i>J. Am. Chem. Soc.</i> (2003) 125(45):13654-13655.	
	FU	WILSON, D. S., et al., "In Vitro Selection Of Functional Nucleic Acids," <i>Annu. Rev. Biochem.</i> (1999) 68:611-647.	
	FV	International Search Report dated November 26, 2004 for International Application No. PCT/US03/34913.	

Examiner Signature	J3 —	Date Considered	4/28/06
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